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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/518,081	03/03/2000	Leland Shapiro	SHAP-000300	5429

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	**PAPER NUMBER**
1656	

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11/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/518,081	SHAPIRO, LELAND	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-17,23-25 and 30-32* is/are pending in the application.

4a) Of the above claim(s) *5,6,8,9 and 23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,10-17 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendments in the Response filed 9 April 2007, to claims 1, 8, 15, and 25, as well as the new claims 31 and 32 have been entered. Claims 5, 6, 8, 9, and 23-25 remain withdrawn form consideration as describing a non-elected invention wherein a claimed method requires a modified peptide inhibitor the nature and structure of which differs substantially from that of the elected polypeptide α1-antitrypsin inhibitor. The claim amendments overcome the objection of record of claim 1 and the rejection of record of claims 1, 3, 4, 7, 10, 12-17, and 30 herein under the second paragraph of 35 U.S.C. § 112.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In *re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 4, 7, 10, 12-17, and 30 remain provisionally rejected for reasons of record on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 6-11, 15, and 34-36 of copending Application No. 10/427,929. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of inhibiting apoptosis in a subject by administering an α1-antitrypsin inhibitor when the subject suffers from any of arthritis, Alzheimer's disease, autoimmune disease, myocardial infarction, stroke, and ischemia-reperfusion injury of the claims pending herein is also a method of treating an animal suffering from induced inflammation by administering an agent exhibiting "mammalian α1-antitrypsin activity" of the copending claims because arthritis, autoimmune disease, myocardial infarction, stroke, and ischemia-reperfusion injury are all well-known to induce inflammation and a preferred agent for administration in methods of all of the copending claims is α1-antitrypsin. See, e.g., the copending claim 36.

Claims 1, 3, 4, 7, 10, 12-17, and 30 remain provisionally rejected for reasons of record on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25, 28, and 29 of copending Application No. 10/669,251. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of inhibiting apoptosis in a subject by administering an α1-antitrypsin inhibitor when the subject suffers from ischemia-reperfusion injury of the claims pending herein is also a method of treating ischemia-reperfusion injury by administering an α1-antitrypsin inhibitor of the copending claims.

These are both provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

While Applicant's Response filed 9 April 2007 requests at page 16 that the issue of nonstatutory obviousness-type double patenting be deferred until an indication of allowable subject matter occurs, the rejections of record must be maintained until and unless a Terminal Disclaimer is filed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 7, 10, 12-17, and 30-32 are rejected, essentially for reasons of record, under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The new claim 31 is included in the rejection of record because its subject matter was previously part of the rejected claim 1. The new claim 32 is included in the rejection of record because is describes subject matter that is, in part, coextensive with the subject matter of the rejected claim 1. Applicant's arguments filed 9 April 2007 have been fully considered but they are not persuasive. The arguments presented at pages 16-18 Response filed 9 April 2007 discuss the issue of enablement in addressing both the rejection of record for lack of adequate written description and the rejection of record for lack of enablement. Separate rejections were made of the elected subject matter under the first paragraph of 35 U.S.C. § 112 and any ambiguity is regretted. The claims were rejected first for lack of an adequate written description in view of the Written Description Guidelines published 5 January 2001, Fed. Reg. 66(4): 1099-1111, which indicate, page 1105, that "[t]he claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The issues presented with regard to written disclosure are (i) whether

the elected serine protease inhibitor α1-antitrypsin is an adequate representative of a broad genus of polypeptide inhibitors that can inhibit apoptosis, a process that exploits many cellular pathways, all intracellular, particularly in view of the diversity of medical conditions recited in claims 1, 31 and 32, which may involve proteases other than serine proteases, and (ii) whether the specification discloses a method wherein the elected species, i.e., the inhibitors recited in claim 3, accomplish, by administration of a "therapeutically effective amount", an inhibition of apoptosis in "a subject . . . suffer[ing] from" one of several diverse medical conditions. The issue of enablement - whether or not the specification provides guidance for administering a serine protease inhibitor to a subject adequate for a therapeutic affect by inhibiting apoptosis, is addressed in a following rejection of record.

The specification fails to exemplify or describe the practice of methods of claims 1, 3, 4, 7, 10, 12-17, and 30 wherein a method of administering the elected serine protease inhibitor α1-antitrypsin to a subject has any affect on the admittedly intracellular pathways of apoptosis – see the discussion at pages 3 and 4 of the specification – by inhibiting cellular serine proteases, metalloproteases, or other proteases. Only Example 6.1 of the specification discusses the administration of α1-antitrypsin to whole animals. i.e., the kind of subjects intended in the claims, but this is a prospective discussion providing no demonstrable results of a reduced level of apoptosis when α1-antitrypsin is delivered to the circulatory system. The specification proposes no proteases other than caspases, granzymes, and cathepsins that may be affected by a serine protease inhibitor, including the elected α1-antitrypsin inhibitor, in its disclosure and these are all intracellular or organelle-conveyed proteases. The specification fails to disclose any method of administration of the α1-antitrypsin inhibitor to a subject that delivers the inhibitor to the cytosolic or nuclear compartments of any mammalian cell that may undergo apoptosis in tissues wherein the medical conditions recited in claim 1 transpire, e.g., neurons, epithelial cells, muscle cells, or connective tissue cells. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of cell-surface or extracellular serine proteases, or any other kind of proteases, that might be the target of a serine protease inhibitor administered to a living animal via its circulatory system, e.g., as in the hypothetical Example 6.1, that might result in an inhibition of apoptosis mediated by proteolytic activity within a cell. The specification fails to disclose a method of administration that might provide the claimed results wherein caspases, granzymes, and cathepsins or other intracellular, or organelle-conveyed, proteases might be

inhibited in order to inhibit apoptosis and treat the medical conditions recited in claim 1, thus the rejection of record is sustained.

Claims 1, 3, 4, 7, 10, 12-17, and 30-32, are rejected, essentially for reasons of record, under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for a method of inhibiting apoptosis mediated by the proteases disclosed in the specification to initiate apoptosis, i.e., caspases, granzymes, and cathepsins, using a serine protease inhibitor to which the cells in tissues affected by the medical conditions recited in claim 1 are impermeable. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice a method of the invention commensurate in scope with these claims.

The new claim 31 is included in the rejection of record because its subject matter was previously part of the rejected claim 1 and the new claim 32 is included in the rejection of record because is describes subject matter that is, in part, coextensive with the subject matter of the rejected claim 1. Applicant's arguments at pages 16-18 of the Response filed 9 April 2007 have been fully considered but they are not persuasive. Applicant does not argue that the specification provides adequate guidance and instead argues that no evidence or technical reasoning was supplied in the communication mailed 9 January 2007. Yet technical reasoning was indeed supplied in that communication, that Applicant declines to discuss with any particularity, and is amplified herein. Claims 1, 3, 4, 7, 10, 12-17, and 30 contemplate a method of administering at least the elected α1-antitrypsin inhibitor to a subject, a term construed according the specification to describe a living organism, producing an inhibition of apoptosis when, according to at least the suggested route of administration proposed in Example 6.1, it is diffused throughout the circulatory system of the subject. The specification does not teach, and the prior art of record herein does not disclose, how to introduce an α1-antitrypsin inhibitor within the cytosolic and nuclear compartments of nervous, muscular, epithelial, or connective tissue cells, i.e., the particular cellular compartments wherein caspases, granzymes, and cathepsins are known to mediate the process of apoptosis, either by the route of administration proposed in the hypothetical example of 6.1 or by any other route of administration. Indeed, if the cells of tissues accessible via the circulatory system were permeable to α1-antitrypsin inhibitor in their native state, including nucleated cells in the blood which are considered to be connective tissue cells, the inhibitor would have to be delivered to at least the cytosolic compartment of such cells at least by diffusion through the cell membrane of cells associated with the diverse conditions recited in claims 1 and 31. The specification nowhere suggests how to deliver α1-antitrypsin inhibitor to cytosolic or nuclear compartments of cells of nervous, muscular, epithelial, or connective tissues in order that it might interact with caspases, granzymes, or cathepsins, and the prior art of record also lacks such a suggestion. Applicant

also argues that the statement of a rejection under 35 U.S.C. § 103 in the communication mailed 5 April 2006 suggests the subject matter of the claims is enabled. The rejection stated in the earlier communication addressed the broad scope of the claims – the set of intended medical results of a claimed method – which need not be mediated by the process of apoptosis, but could be mediated by the administration of α1-antitrypsin inhibitor to affect a non-cellular process, and the amendment of the claim to delete the particular result rejected is considered to agree with such a broad construction of the scope of the claims. The rejection of record is therefore sustained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/Nashed/
Nashaat T. Nashed, Ph.D.
Primary Examiner, Art Unit 1656

William W. Moore
21 November 2007